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Case review

Primary pulmonary rhabdomyosarcoma with brain metastases in a child: A case report with medico-legal implications

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ABSTRACT

Rhabdomyosarcoma (RMS) is a rare type of soft tissue sarcoma that mainly affects children. RMS in childhood commonly occurs in the head and neck, followed by the genitourinary tract. Primary pulmonary rhabdomyosarcoma (PPR) is extremely rare. We report a 31-month-old girl who had PPR with brain metastasis. The girl with wheezing and cough of 3 weeks and vomiting of 1 day was referred to a county hospital. At 9:00 a.m., a chest X-ray showed an abnormal shadow on a chest radiogram. Four hours later, in the process of computed tomography (CT) scan her condition deteriorated dramatically, while resuscitation efforts were unsuccessful. CT showed a solid mass in the right middle lung lobe. Subsequent autopsy revealed a large tumour located in the right middle lung lobe. Surprisingly, a mass of haematoma appearance was found in the left occipital lobe. Histological and immunohistochemical investigations of the masses established the diagnosis of PPR with brain metastasis. Herniation of brain, caused by the brain metastasis, was ascertained as the cause of death. The morphological and pathological findings are presented; the difficulty to diagnose PPR and the medico-legal implications are discussed.

1. Introduction

Rhabdomyosarcoma (RMS) is an extremely rare type of soft tissue sarcoma that is thought to derive from mesenchymal stem cells and shows varying degrees of skeletal muscle differentiation.[1] Primary pulmonary rhabdomyosarcoma (PPR) has been sporadically reported in spite of the fact that the lung is devoid of striated muscle.[2] Since the first case of PPR was reported in 1939,[3] there have been only 39 cases in the available English world literature (22 in children and 17 in adults).[2,4–6] Cerebral metastasis as the initial manifestation of RMS is a rare event. Such a seldom-seen case can easily trigger medical disputes, especially in countries such as China with increasing malpractices, medical negligences and lawsuits.[7] Furthermore, the one-child policy in China makes the medical disputes involving children even tougher.[8] Therefore, it is of great significance for us to report the case of a 31-month-old girl who had PPR with brain metastasis. In the literature, there are only a few case reports concerning PPR as an unexpected cause of death and, as far as we know, no other articles focussed on the medico-legal implications of such case.

2. Case report

A 31-month-old girl presented with a 3-week history of wheezing and a croupy cough. Admission to the hospital was precipitated by worsening of her symptoms, including tachypnoea and vomiting. Haemogram, urinalysis and a chemistry profile revealed no abnormalities. A chest X-ray showed a large tumour in the right middle lung lobe (Fig. 1A). In the process of computed tomography (CT) scan, her condition deteriorated dramatically and resuscitation efforts were unsuccessful. CT of the chest confirmed the latter finding as well as a large solid mass being noted (Fig. 1B and C).

In this case, the child expired 4 h after admission. Parents of the girl believed that the necessary assist examination delayed the cure. Due to the lack of clinical experience and knowledge as well as patients' low confidence in doctors, this case was sent to our judicial identification centre for forensic identification (Hunan

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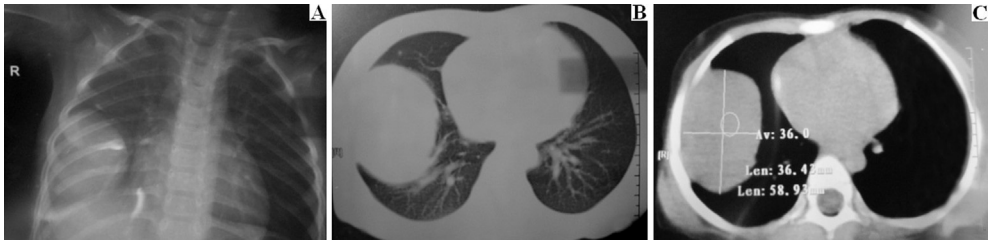

Fig. 1. (A) Chest radiogram at the time of admission shows a huge tumour in the right middle lung. (B) Computerized tomography scan shows a large solid mass in the left middle lobe. (C) Contrast-enhanced computed tomography revealed a large solid mass lesion (58 mm × 36 mm) involving the anterior segment of the left upper lobe.

Xiang Ya judicial identification centre). Medico-legal autopsy was ordered by the prosecutor due to complaints of medical negligence.

3. Autopsy findings

External examination revealed an asthenic habitus (body weight 10 kg, height 85 cm). External examination of the body did not show any evidence of significant trauma. The findings regarding internal organs were according to the age of the patient except the brain and lungs. The left lung was soft and normal. A large tumour located in the right middle lung lobe. The mass (5.8 × 3.7 × 3.6 cm) was irregularly oval in shape. On section of the right middle lobe the tumour replaced >90% of the lobe and the adjacent lung was focally atelectatic. It was relatively well circumscribed and partially surrounded by compressed lung, particularly over tire lateral aspect of the lobe. The tumour was soft and creamy white with large areas of necrosis and haemorrhage (Fig. 2A). None of the pulmonary hilar lymph nodes was involved, although some nodes were surrounded by the tumour. Cerebral oedema and tonsillar hernia were disclosed. A mass of haematoma appearance (4.5 × 4.0 × 3.0 cm) was found in the left occipital lobe (Fig. 2B). The cut surface showed many haemorrhagic and necrotic areas (Fig. 2C).

Microscopic examination of primary and metastatic neoplasm reveals essentially the same histopathologic appearance. The neoplasm is pleomorphic without an organised pattern. It is composed of sheets of cells varying from round to polyhedral to spindle in configuration with occasional straplike cells. The cells vary greatly in size and somewhat vesicular nuclei with occasional prominent nucleoli. The amount of cytoplasm is variable and is pale to eosinophilic. There were also many abnormal mitoses. Tumour tissue was continuous with the lung alveolar structures, with no interposition of dividing collagenous septa. A few more differentiated tumour cells, which had abundant eosinophilic cytoplasm and monstrous, bizarre nuclei with prominent nucleoli, showed cross-striations (Fig. 3A). Mitotic figures were frequently observed up to 14 per 10 high-power fields. Immunohistochemical stains showed diffuse positivity for myogenin (Fig. 3B) and focal positivity for vimentin, desmin and striated muscle actin (Fig. 3C). Stains for glial fibrillary acidic portein (GFAP), smooth muscle actin, CK-pan and S-100 protein were negative (Fig. 3D). No significant change appeared in histopathologic morphology between tumours located in brain and lung. A diagnosis of pulmonary embryonal RMS (ERMS) with brain metastasis was made. There was no evidence of any abnormalities in other organ systems. Post-mortem toxicological analysis was negative for drugs. Herniation of brain, caused by the brain metastasis, was ascertained as the cause of death.

4. Discussion

RMS originates from the embryonal mesenchyme that ultimately gives rise to striated skeletal muscle.[9] RMS occurs predominantly in children <7 years, has a second age peak in adolescence and the incidence subsequently declines in older patients.[10] PPR is extremely rare and, according to previous reports, two main distinguishable histological subtypes that affect both adults and children are ERMS and alveolar RMS (ARMS).[11] The third subtype, pleomorphic RMS, occurs almost exclusively in adults, and there is growing evidence that this tumour type should be biologically considered rather a distinct type of adulthood soft tissue sarcoma than a subtype of RMS.[12]

RMSs arising in the lung or brain are of particular interest, since striated muscle is scanty or absent in these sites in normal individuals. The diagnosis of RMS depends on the histological examination and is based on the characteristic finding of cross-striations in the cytoplasm of tumour cells. Histological diagnosis is the cornerstone in establishing the diagnosis and making the consequential treatment decisions in PPR. Still, histopathological diagnosis of PPR is a challenge. The greatest diagnostic challenge in this case is the distinction from other poorly differentiated small

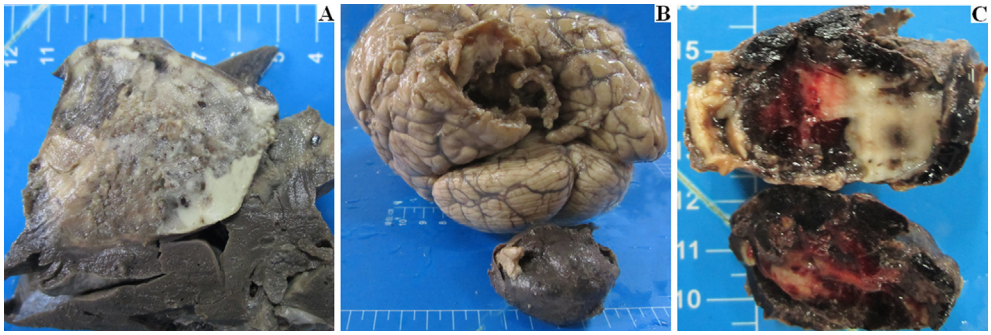

Fig. 2. (A) A 5.8 × 3.7 × 3.6-cm mass was located in the right middle lung lobe. (B) A 4.5 × 4.0 × 3.0 -cm mass of haematoma appearance was out of the left occipital lobe. (C) The cut surface of the mass was located in the left occipital lobe.

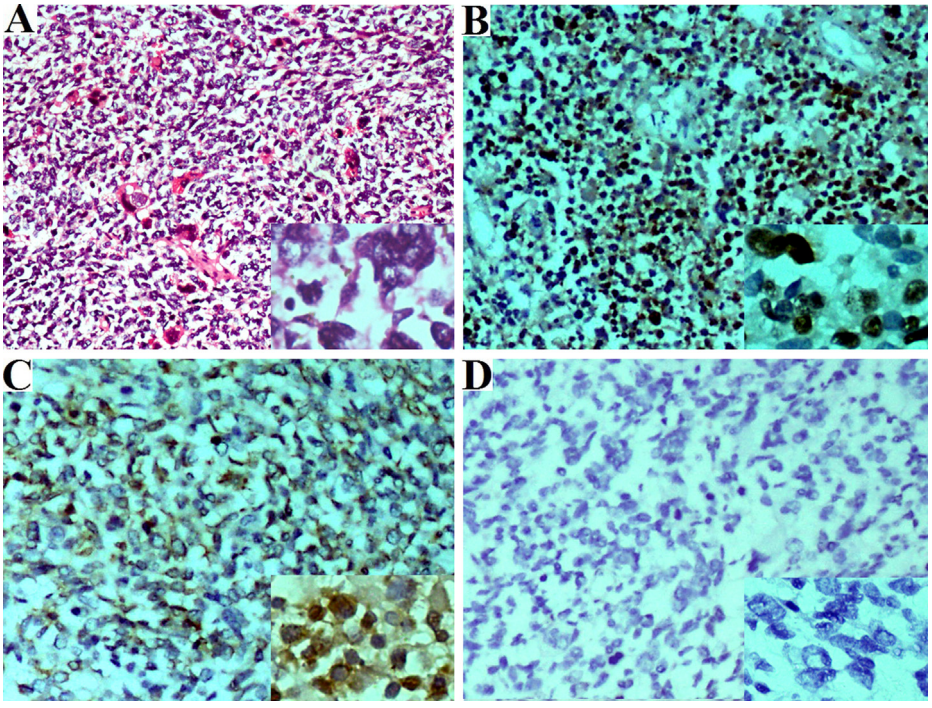

Fig. 3. (A) PPR composed of highly cellular and pleomorphic cells. Inset, several mitoses are seen in one high power field. (Haematoxylin and eosin stain, × 100. Inset, × 400.) (B) Diffuse immunoreactivity of tumor cells to myogenin. (Immunohistochemistry, × 100. Inset, × 400.) (C) Immunohistochemical stains showed focal positivity for vimentin (Immunohistochemistry, × 100. Inset, × 400.), and positive immunostaining of desmin and striated muscle actin were similar with vimentin. (D) Stains for smooth muscle actin were negative. (Immunohistochemistry, × 100. Inset, × 400.)

blue round-cell tumours, including neuroblastomas, Ewing's sarcoma and primitive neuroectodermal tumours. Immunohistochemically, RMS shows intranuclear expression of the myoregulatory proteins myogenin.[13] In this case, myogenin shows the highest specificity and sensitivity (Fig. 3B).

It has been reported that the prevalence of cerebral metastasis is increased in sarcoma patients experiencing a prolonged response to chemotherapy.[14] However, in this case, brain metastasis happened without any therapy. Central nervous system (CNS) spread from any form of sarcoma is uncommon, and CNS metastasis from embryonal RMS is also uncommon, being seen in only 2/85 cases in one series.[15] Furthermore, intracerebral haemorrhage is a particularly unusual initial presentation of metastatic RMS.

Generally speaking, death due to herniation of brain caused by PPR with brain metastasis was a rather rare event. With the enhancement of public legal awareness and the improvement of China's legal system, the legal issues in medical practice have attracted more and more attention. Of all kinds of reasons, the most important are the mistrust between the patients and the hospitals. An authoritative medical damage identification system should be established to guarantee the verdict of identification to be real, scientific, objective and just. If an infant's sudden death took place and the parents complained about medical negligence, a detailed report along with autopsy is necessary to clarify the fact. In this case, the girl's autopsy report facilitated a speedy reconciliation between the parents and the hospital.

In conclusion, we presented an autopsy case of sudden unexpected death due to an extremely rare type of RMS that arose from pulmonary. The diagnosis of the PPR was established by post-mortem pathological examination. PPR is an extremely rare disease, and because of its early metastasis, the prognosis of it is poor. PPR should be included in consideration in the diagnosis and differential diagnosis of lung tumours. Meanwhile, forensic autopsy is further proved to be the reliable standard to identify the cause of death in individuals who die suddenly and unexpectedly.

Ethical approval

None.

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Conflict of interest

None.

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